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Single sweep three-dimensional carotid ultrasound: Reproducibility in plaque and artery volume measurements

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ABSTRACT

Background: There is a need for non-invasive and accurate techniques for assessment of severity of atherosclerotic disease in the carotid arteries. Recently an automated single sweep three-dimensional ultrasound (3D US) technique became available. The aims of this study were to evaluate the feasibility and reproducibility of the automated single sweep method in a cohort of patients undergoing clinically indicated carotid ultrasound.

Methods: Consecutive patients with a history of stroke or transient ischemic attack (TIA) and having a plaque in the internal carotid artery (ICA) were recruited for this study. Imaging was performed using a Philips iU 22 ultrasound system equipped with the single sweep volumetric transducer vL 13-5. Analysis was performed offline with software provided by the manufacturer. Two independent observers performed all measurements.

Results: Of 137 arteries studied (from 79 patients), plaque and artery volumes could be measured in 106 (77%). Reproducibility of plaque volume measurements was assessed in 82 arteries. Bland–Altman analysis demonstrated good inter-observer reproducibility with limits of agreement −0.06 to +0.07 ml. The mean percentage difference between two observers was 5.6% ± 6.0%. Reproducibility of artery volume measurement was assessed in 31 cases. Bland–Altman analysis demonstrated limits of agreement from −0.15 to +0.15 ml. The mean percentage difference was 6.4 ± 5.9%.

Conclusion: The new automated single sweep 3D ultrasound is feasible in the majority of patients. Good reproducibility in plaque and artery volume measurements makes this technique suitable for serial assessment of carotid plaques.

1. Background

Two-dimensional ultrasound (2D US) with color and spectral Doppler remains the non-invasive method of choice for the assessment of carotid atherosclerosis. It is used to estimate risk of ischemic cardiovascular events by measurement of the carotid intima-media thickness (CIMT) [1–3] and to quantify the severity of carotid artery stenosis in patients who have suffered ischemic stroke or transient ischemic attack (TIA) [4–6]. Nevertheless, these measures have some limitations. The prognostic utility of CIMT as a marker of risk has recently been questioned in a large meta-analysis [7]. Assessment of stenosis by 2D methods is also subject to error: Doppler measurements are susceptible to a variety of technical and hemodynamic factors meaning the technique is operator-dependent and may vary further between different machines and manufacturers [8].

There is therefore a continuing need to improve methods of carotid stenosis and plaque assessment by ultrasound. One of the most promising advances in recent years has been the development of three-dimensional (3D) imaging techniques. Recent work has explored the role of 3D US in the evaluation of carotid plaque volume, degree of stenosis, plaque morphology or composition, and progression over time [9].

A variety of 3D acquisition methods have been described, mostly using a free-hand technique. This involves translation of the

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transducer over the artery while 2D images are acquired to form a volumetric dataset. Some methods require an external carriage motion device and magnetic field sensor to identify the relationship of the probe to the artery [10]. These techniques are relatively complex and time-consuming, and none are currently used in daily clinical practice.

More recently, an automated single sweep 3D imaging method has been developed, allowing acquisition from a stable probe position. The ultrasound beam is steered automatically through the area of interest allowing greater ease of imaging and reduced scanning time. Measures of plaque and arterial volume can be calculated using off-line software, as previously described by our group [11] and others [12].

The aims of this study were to evaluate the feasibility and reproducibility of the automated single sweep method in a cohort of patients undergoing clinically indicated carotid ultrasound.

2. Methods

2.1. Study sample

Seventy-nine consecutive patients referred for carotid ultrasound were recruited following a diagnosis of stroke or TIA. In all patients both carotid arteries were scanned. Arteries with plaque extending beyond the internal carotid artery (ICA), with complete ICA occlusion and those with multiple ICA plaques were excluded. Plaques longer than 4.5 cm also were excluded, as this exceeds the maximum length the transducer can acquire. Conventional B-mode, color and pulse wave Doppler, and 3D carotid ultrasound scanning were performed at the University of Alberta Hospital Stroke Prevention Clinic by an experienced sonographer and a physician. The study was approved by University of Alberta Health Research Ethics Board – Health Panel, Study ID: Pro00031031.

2.2. 2D carotid ultrasound

Recording and analysis of conventional (2D) ultrasound studies were performed according to recommendations of the American Society of Echocardiography [13] using the Philips iU 22 ultrasound machine (Philips Health Care, Andover, MA) with an L 9-3 linear transducer. The degree of carotid artery stenosis was determined according to the Consensus Statement [8] using gray-scale and Doppler US.

2.3. Automated single sweep method of the 3D data acquisition

Three-dimensional carotid ultrasound was performed using a Philips iU 22 ultrasound system equipped with the single sweep volumetric transducer (vL 13-5). The transducer was maintained in a single position parallel to the long axis of the artery. The ultrasound beam is steered automatically through a 10° sagittal arc according to a predefined region of interest, incorporating the common carotid artery (CCA), bulb of the ICA, and the middle ICA. Using this method the entire 3D dataset was acquired in less than 2 s. The steps of 3D data acquisition are presented in Fig. 1. In this way, a volumetric dataset was acquired for reconstruction into multi-planar and volume-rendered images (Fig. 2).

2.4. Measurement of plaque and artery volumes

Orthogonal longitudinal, transverse, and coronal planes were reconstructed offline using Philips Q-Lab analysis software. Quantification of plaque and artery volumes was performed using a method of disks similar to that used for assessing left ventricular volumes at echocardiography [14]. Briefly described, the method of

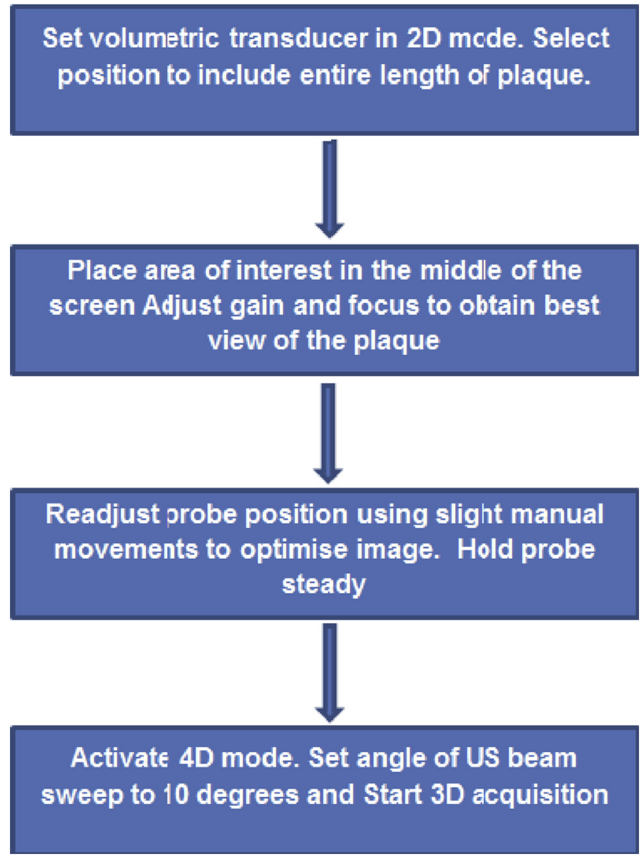

Fig. 1. Flow chart of 3D dataset acquisition steps.

"stacked-ellipses" employs a circular or ellipsoid template to assign artery boundaries (instead of manual tracing), following which the borders can be adjusted to delineate the plaque. This method is particularly useful for extrapolating borders of the carotid artery on the transverse view when they are not completely seen (see below). However, the software has no particular advantage in lumen–intima and media–adventitia boundary detection compared to software employed in previous 3D ultrasound studies.

The protocol of plaque and artery volume measurement involves several steps. The maximal length of the plaque is measured on the sagittal view, defined as "Distance" (the blue dashed line in Fig. 3). Using the stacked ellipses tool, consecutive transverse slices are generated from the cranial to caudal edges of the plaque (Fig. 4A). Depending on the plaque length, the number of slices can be increased to a maximum of 15 by altering the inter-slice distance (ISD) [15]. Assuming a regular shape of the artery, circular templates are aligned to inner borders of the common and internal carotid artery walls (Fig. 4A, B and C) and adjusted manually. Where an adequate fit cannot be achieved, an ellipsoid shape can be substituted, which may be more accurate for delineation of the bulb of ICA. Where vessel borders are difficult to define in the transverse view, for example in arteries with an irregular surface, appropriate placement of contours is confirmed by assessing from the longitudinal image, generated simultaneously as a dashed yellow line. After tracing all consecutive slices, the segmental arterial volume is calculated as the sum of each slice volume, by slice area and ISD.

Plaque volume is measured in a similar manner; the borders are traced within the artery lumen by manually altering the previously delineated arterial borders (Fig. 5A, B and C). However, given the irregular shape of the plaques, a smaller inter-slice distance (1–2 mm) is used to increase the accuracy of volume

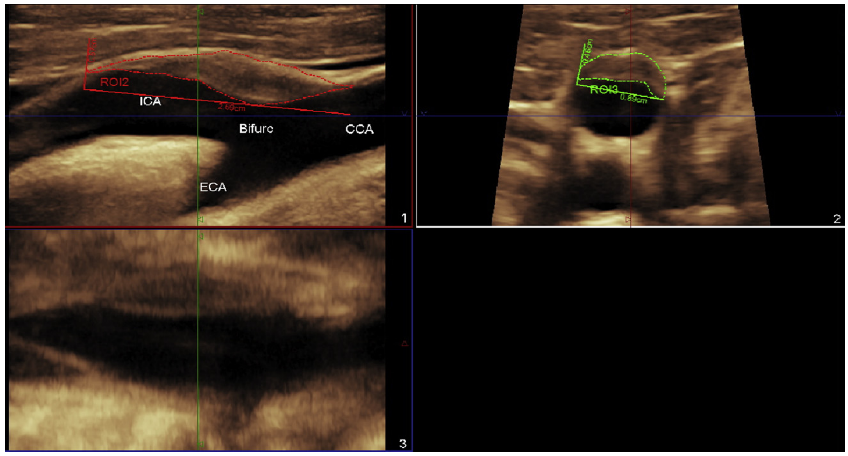

Fig. 2. Reconstructed 3D dataset. The upper-left image is the sagittal view of the carotid artery. The green vertical line indicates the slice of the ICA corresponding to the transverse view on the upper-right image. The bottom-left is the volume-rendered image. The plaque on the sagittal view is delineated with red line and with the green one on the transverse slice. ICA = Internal Carotid Artery, Bifurc = Bifurcation, ECA = External Carotid Artery, CCA = Common Carotid Artery. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

measurements. The time required to perform these steps, calculating both plaque and segmental arterial volumes, was less than 10 min.

To assess inter-observer variability, 2 independent observers performed measurements of plaque and artery volumes, blinded to the results of the other.

2.5. Statistics

Demographic data are displayed using mean and standard deviation (SD). The Bland–Altman test [16,17] and mean percentage change [18] were used to determine inter-observer variability in plaque and artery volumes calculations. IBM SPSS Statistics (Version 21.0. Armonk, NY: IBM Corp) and Analyse-it software (http://www.analyse-it.com/; 2009) were used for statistical analyses.

3. Results

Of 79 patients studied 48 (61%) were men, with a mean age of 68 ± 10 years. Clinical parameters of study patients are presented in Table 1. Twenty one arteries were not included in analysis due to absence of plaque or extension of plaque beyond the ICA. Of 137 arteries studied, plaque and artery volumes could be measured in 106 (77%). Accurate assessment was impossible in the remaining 31 cases, mainly due to the presence of heavy calcification and acoustic shadowing. In a small number of cases this was due to hypo-echogenic plaques such that the inner lumen could not be visualized accurately on B mode. The mean plaque volume was 0.44 ± 0.29 ml (range 0.05–1.67 ml). The mean artery segmental volume was 1.08 ± 0.58 ml (range 0.19–3.20 ml).

3.1. Reproducibility of plaque and artery volume measurements

Reproducibility of plaque volume measurements was assessed in 82 arteries (Fig. 6A). Bland–Altman analysis demonstrated good inter-observer reproducibility with limits of agreement from −0.06 to +0.07 ml, bias = 0.005 ml, and SD of differences between single measurements = 0.03 ml.

The mean percentage change between measurements of both observers was also calculated. This refers to the absolute difference between the observers' volumes relative to their mean [18], calculated as ({Obs1 − Obs2}/(Obs1 + Obs2)/2) × 100. The mean percentage change for plaque volume measurements was 5.6 ± 6.0%.

Reproducibility of artery volume measurements was assessed in 31 arteries (Fig. 6B). Bland–Altman analysis demonstrated limits of agreement from −0.15 to +0.15 ml, bias = 0.00 ml, and SD of differences between single measurements = 0.08 ml. The mean percentage change for artery volume measurements was 6.4 ± 5.9%.

4. Discussion

The results of this study demonstrate the feasibility of plaque and artery volume assessment in a majority of patients referred for clinically indicated carotid ultrasound. Furthermore, the methods described in this study for 3D acquisition and analyses provide highly reproducible measures of plaque and artery volume.

2D carotid US is most frequently performed for risk stratification to guide intervention in patients who have experienced recent ischemic stroke or TIA. However, this technique depends on Doppler measures which are prone to a variety of technical and

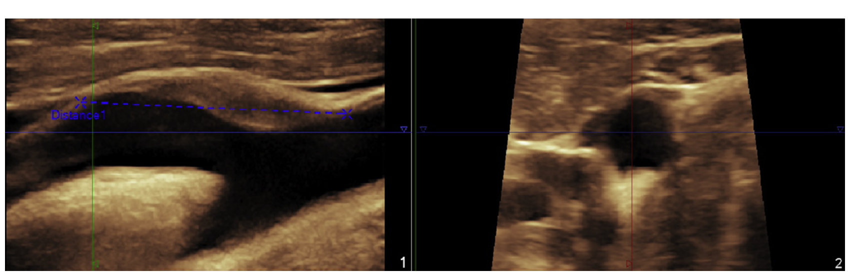

Fig. 3. First step of the measurements: defining the longest plaque length illustrated by dashed blue line (distance). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

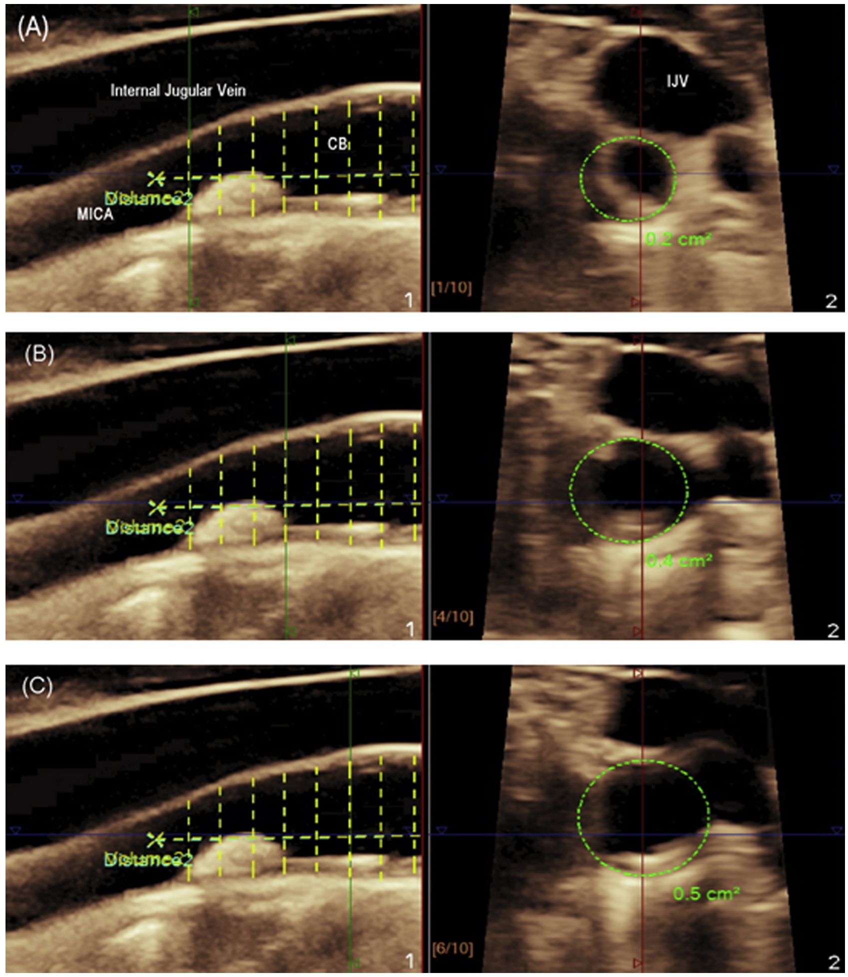

Fig. 4. Steps of segmental arterial volumetric measurement from the 3-dimensional dataset. Measurements from the 1st (A), 4th (B), and 6th (C) slices out of 10 are shown. Images on the left are longitudinal views with the corresponding transverse views on the right side. The green lines in the longitudinal (left sided) images indicate the positions where the transverse slices were taken. The yellow dashed lines indicate the consecutive slices used for calculation of the segmental vessel volume. The green circles on the right (the transverse views), indicate circumferential arterial surface area measurements. CB = carotid bulb, MICA = middle part of internal carotid artery, IJV = internal jugular vein. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

hemodynamic factors such as insonation angle, cardiac output, and presence of sequential or bilateral carotid stenoses. Therefore, acquisition and interpretation of results can differ considerably from one vascular laboratory to another, requiring quality assessment and internal validation within each institution [19–21]. Where uncertainty exists, it may require verification by other techniques including magnetic resonance angiography (MRA), computed tomographic angiography (CTA), or digital subtraction angiography (DSA) [22–25].

Using conventional two-dimensional ultrasound, the severity of atherosclerosis has also been assessed by measurement of carotid intima-media thickness (CIMT) [1–3]. However, accumulating data have suggested that CIMT is not an accurate marker of atherosclerosis. CIMT and atherosclerotic plaque have been shown to be biologically and genetically distinct entities and respond differently to therapies [26,27]. In a recent large meta-analysis the extent of carotid plaque, when compared to CIMT, showed a greater accuracy for the prediction of future coronary ischemic events [7].

While the role of 3D US in carotid assessment is still evolving, the development of 3D methods for this purpose has been continuing for a number of years. Initial studies of 3D carotid imaging were performed in the early 1990s [28], with measurement of carotid plaque volume initially described in 1994 [29] and developed further with the introduction of manual planimetry [30–32]. One of the main advantages of the current method is the ease and speed of image acquisition – the volumetric dataset is acquired automatically from a stable probe position in less than 2 s. Nevertheless, clinical studies assessing the utility of this method are presently limited.

Johri and colleagues examined the relationship between carotid plaque volume and severity of coronary artery disease in a cohort of patients referred for coronary angiography [12]. Plaque volume obtained using the single sweep 3D method with stacked contours was superior to 2D plaque thickness in predicting the absence of significant coronary artery disease. The investigators reported reproducibility in 10 patients with an inter-rater reliability for classification ($k = 0.912$). However, the absolute difference between the measurements of two observers was not reported. This figure may be more important, especially if these techniques were applied to sequential measurements of carotid plaque in interventional trials.

Accurate assessment of atherosclerotic burden is an important measure where progression or regression of plaque is used to assess the relative impact of atherogenic risk factors, or therapeutic intervention. One follow-up study of patients with type 2 diabetes has demonstrated the superiority of plaque volumes over CIMT as a

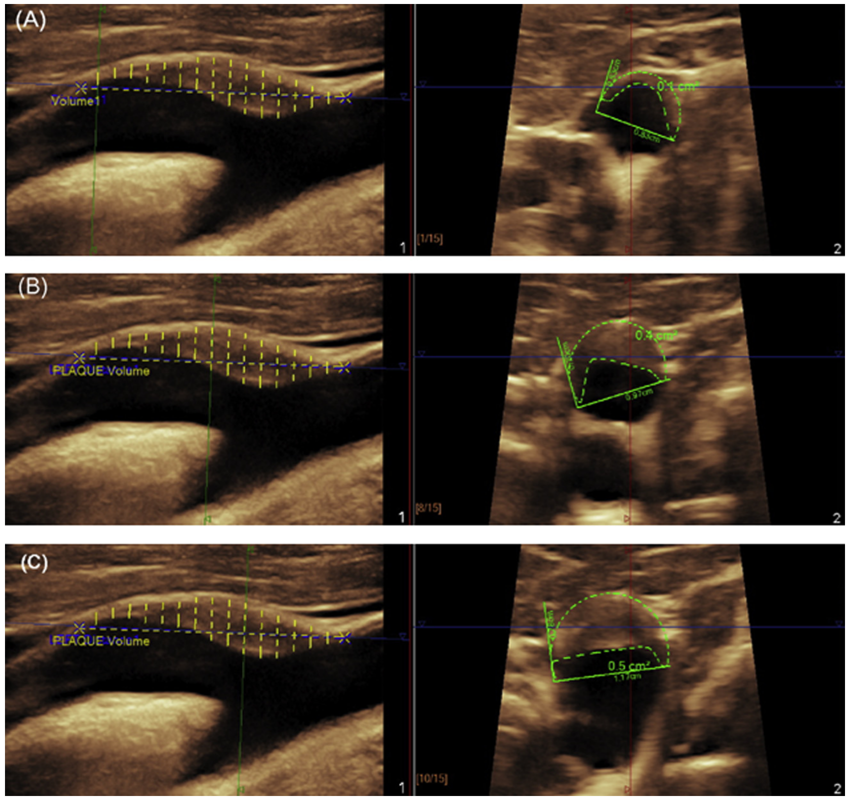

Fig. 5. Steps of plaque volume measurement from the 3-dimensional datasets. The measurements of 1st (A), 8th (B), and 10th (C) of 15 slices are shown. Plaque borders are identified within the lumen of the artery by manually altering the previously delineated borders of arterial circumference. This is performed by dragging the circumferential line towards the plaque borders.

marker of atherosclerosis progression over 7 years [33]. This may relate to differences in the pathology of plaque and CIMT progression, as well as the difficulties in accurate and reproducible measurement of CIMT as compared to plaque volume.

Previous studies have shown the feasibility of 3D ultrasound in depicting changes in carotid plaque volume, with a change in volume of 20–30% considered significant [33–38]. Both progression and regression have been observed by these studies with or without treatment. However, sample sizes, duration of follow-up and reported plaque volume changes varied markedly between them.

Inter-observer correlation may also vary with plaque progression or regression and the current study design did not include provision for follow-up of these patients. However, using a cut-off of 2 standard deviations in mean percentage change, the results suggest the 3D single sweep method could confidently detect a change in plaque volume of 12% in an individual. A broad variety of plaque size, morphology and echogenicity was encountered, including those with calcification and ulceration. We therefore think that the reproducibility demonstrated in this study represents the variety of disease encountered in clinical practice.

In this study, the inter-observer reproducibility was 5.64%, assessed by mean percentage change. This is comparable to levels

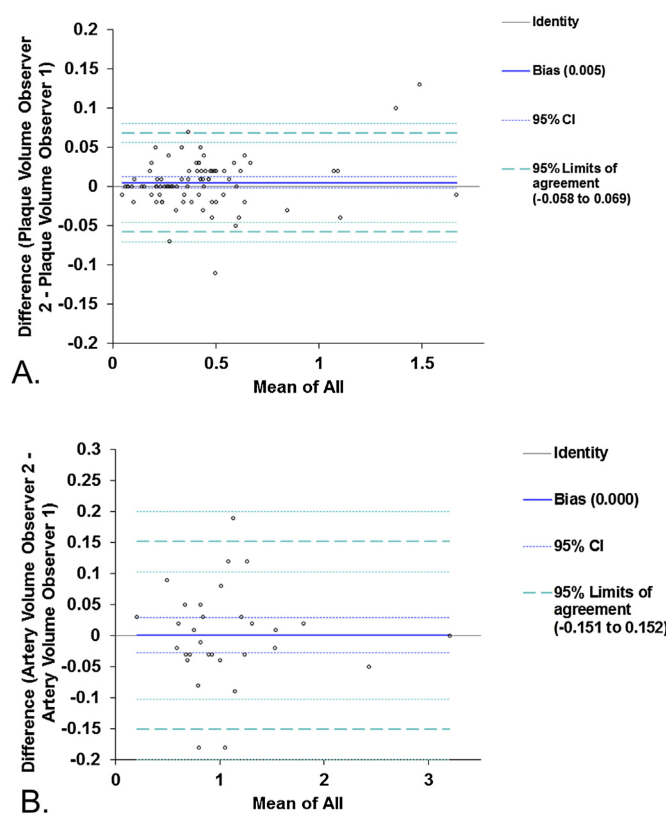

Fig. 6. Inter-observer variability for plaque volume measurement (A) and artery volume measurement (B) using Bland–Altman analysis.

Table 1
Clinical parameters of the study patients.

	Total ($n = 79$)	Male ($n = 48$)	Female ($n = 31$)
Hypertension	57 (72.2%)	35 (72.9%)	22 (71.0%)
Diabetes	16 (20.3%)	13 (27.1%)	3 (9.7%)
Dyslipidemia	61 (77.2%)	36 (75.0%)	25 (80.6%)

of agreement quoted by other studies assessing more cumbersome methods for 3D dataset acquisition and analysis, with inter-observer variability ranging from 4.2 to 7.6% for plaque volumes [9,15,29,33,39]. The good inter-observer agreement demonstrated in the current study suggests the single sweep 3D method is suitable for the study of carotid atherosclerosis in clinical practice, and may allow its implementation for follow-up of plaque volume changes. The clinical utility of plaque volume measurement, and its relative prognostic utility compared to currently used 2D measures of carotid stenosis remains to be established in clinical studies.

5. Conclusion

Assessment of carotid plaque by the automated single sweep 3D method is feasible in the majority of patients referred for carotid ultrasound, and shows good reproducibility in plaque and artery volume measurements. The speed of acquisition and simplicity of the volumetric measurements is a further advantage, and this method warrants investigation to ascertain its utility in future prognostic and interventional studies.

Conflict of interest

All authors have no conflict of interest to declare.

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